Applicant: Anthony J.F. D'Apice et al.

Serial No.: 08/984,900

Filed: December 4, 1997

Page : 2

more conservative amino acid substitutions, wherein said second polypeptide retains a functional  $\alpha$ -1,3 galactosyltransferase catalytic site, a functional membrane anchor domain and a functional stem region, and (4) a sequence complementary to the sequence of (1), (2) or (3).

Attorney's Docket No.: 06868-005002

3. (Amended) A porcine  $\alpha$ -1,3 galactosyltransferase encoded by the nucleic acid molecule of claim [2]  $\underline{1}$ .

- 46. (Amended) A DNA construct comprising a disrupted porcine  $\alpha$ -1,3 galactosyltransferase gene, wherein the gene, prior to disruption, encodes a porcine  $\alpha$ -1,3 galactosyltransferase with an amino acid sequence of SEQ ID NO:10 and wherein the disruption is by [the] insertion of an exogenous sequence into said gene such that the disruption prevents expression of functional  $\alpha$ -1,3 galactosyltransferase.
- 54.  $\frac{3}{5}$ . (Amended) A method for generating a porcine cell comprising at least one inactivated  $\alpha$ -1,3 galactosyltransferase gene, the method comprising:
  - (a) providing a plurality of porcine cells;
  - (b) introducing into said cells [a DNA construct comprising a disrupted porcine  $\alpha$ -1,3 galactosyltransferase gene, wherein the disruption is by the insertion of an exogenous sequence into said gene such that the disruption prevents expression of functional  $\alpha$ -1,3 galactosyltransferase] the DNA construct of claim 46;
  - (c) incubating said cells such that homologous recombination occurs between the chromosomal sequence encoding  $\alpha$ -1,3 galactosyltransferase and the introduced DNA construct comprising the disrupted  $\alpha$ -1,3 galactosyltransferase gene; and
  - (d) identifying a porcine cell comprising at least one inactivated  $\alpha$ -1,3 galactosyltransferase gene.
  - 67. (Twice amended) A porcine cell comprising at least one disrupted  $\alpha$ -1,3 galactosyltransferase gene, wherein the disruption is by insertion of an exogenous sequence into said gene such that the disruption prevents expression of functional  $\alpha$ -1,3 galactosyltransferase

Applicant : Anthony J.F. D'Apice et al.

Serial No. : 08/984,900

Filed Decemb

December 4, 1997

Page

: 3

and wherein the gene, prior to disruption, encodes the porcine  $\alpha$ -1,3 galactosyltransferase with an amino acid sequence of SEQ ID NO:10.

Attorney's Docket No.: 06868-005002

70. (Twice amended) The porcine cell of claim [68]  $\underline{67}$ , wherein said disruption is within exon 4, exon 7, exon 8, or exon 9 of the porcine  $\alpha$ -1,3 galactosyltransferase gene.

- 71. (Twice amended) The porcine cell of claim [68] <u>67</u>, wherein said exogenous sequence is a selectable marker.
- 72. (Twice amended) The porcine cell of claim [70] <u>71</u>, wherein said selectable marker is selected from the group consisting of the neo<sup>R</sup> gene and the hyg<sup>R</sup> gene.
- 73. (Twice amended) The porcine cell of claim [68] <u>67</u>, wherein said exogenous sequence is flanked at its 5' and 3' ends by FRT DNA elements, and wherein stop codons have been inserted 3' to the selectable marker for each of the three reading frames for the porcine  $\alpha$ -1,3 galactosyltransferase gene.

Add new claims 74-77.

- --74. The method of claim 51, wherein said disruption is within exon 4, exon 7, exon 8, or exon 9 of the porcine  $\alpha$ -1,3 galactosyltransferase gene.
  - 75. The method of claim 51, wherein said exogenous sequence is a selectable marker.
- 76. The method of claim 75, wherein said selectable marker is selected from the group consisting of the neo<sup>R</sup> gene and the hyg<sup>R</sup> gene.